REMARKS

I. The Subject Matter of the Claims

In general, the subject matter of the claims relates to monoclonal antibodies specifically reactive with α_d integrin which modulate TNFα activity.

II. The Objections to the Specification

Applicants note the Examiner's objection regarding the formal drawings and will submit final drawings upon notification of allowance.

III. Patentability Arguments

A. The Rejection of Claims 11, 12 and 14 under 35 U.S.C. §102(b), May Properly be Withdrawn.

The Examiner maintains the rejection of claims 11, 12 and 14 under 35 U.S.C. §102(b) as assertedly anticipated by Gallatin, which allegedly teaches methods of treating immune or inflammatory responses with antibodies to α_d. The Examiner asserts that inhibition of TNFα activity from macrophages or splenic phagocytes is an inherent property of the antibodies disclosed by Gallatin.

Applicants respectfully disagree. The Examiner has overlooked the statements submitted in Applicant's response of December 29, 2004, that nothing in the Gallatin disclosure definitively indicates that the molecule identified in Gallatin as integrin α_d is present on macrophages or splenic phagocytes *in vivo*. Gallatin, column 5, paragraph 5, states that <u>if</u> α_d is found on macrophages, it may allow for development of therapeutics to several immune diseases, such as atherosclerosis or multiple sclerosis. The disclosure proceeds to describe cloning of a polynucleotide encoding a putative homolog of the canine protein, calling it human

α_d, but does not confirm its expression on macrophage cells. Northern blot experiments teach that there is weak α_d signal from several human tissue sources, none of the tissue sources being spleen tissue. Col. 14, lines 13-28. Although α_d was isolated from a spleen cDNA library, Gallatin does not indicate that it was localized in the spleen. Further, Gallatin also demonstrates only weak α_d expression seen in "macrophage" or "monocyte" cell lines, either before or after stimulation of the cells. None of this evidence is convincing to a worker of ordinary skill that α_d is a macrophage or splenic phagocyte *specific* cell surface antigen.

Moreover, Gallatin cautions that absent sequence information, a definitive correlation between human integrin subunits and those identified in other species has not been possible. Col 1, lines 56-60. Gallatin discloses only ~1000 nucleotides of the canine sequence used to isolate a 3726 nucleotide human clone, compare SEQ ID NO: 24 and 1, respectively. The human α_d protein is 1161 amino acids in length (SEQ ID NO: 2), whereas the encoded canine polypeptide, which was not identified, would be at most ~330 amino acids. This information was insufficient to allow the Gallatin authors to definitively state that the human α_d is a homolog of the canine protein.

For a reference to anticipate, that single reference must disclose each and every limitation of the claimed invention, in the arrangement as specified in the claim. MPEP 2131. The present invention involves methods for specifically inhibiting TNFα activity from macrophages or splenic phagocytes using monoclonal antibodies to integrin α_d. Gallatin neither discloses nor suggests any ability of α_d-specific antibodies to modulate macrophage or splenic phagocyte activity, especially when it was not disclosed that the α_d protein was on these particular cell populations. Gallatin simply describes a method for producing antibodies to a newly identified protein, and discloses a general use for the disclosed antibodies, without giving

any particular examples of α_d-specific monoclonal antibodies or methods for their use, other than a generic use for treating immune or inflammatory responses.

Because Gallatin does not disclose that the α_d protein is specifically expressed on human macrophage populations, a worker of ordinary skill in the art would not have predicted that α_d would modulate TNF-α release from these cells. Thus, Applicants submit that the rejection of claims 11, 12 and 14 under 35 U.S.C. § 102(b) should properly be withdrawn.

IV. Conclusion

In view of the amendments and remarks made herein, Applicants submit that claims 11, 12 and 14 are in condition for allowance and respectfully request expedited notification of the same.

Respectfully submitted,

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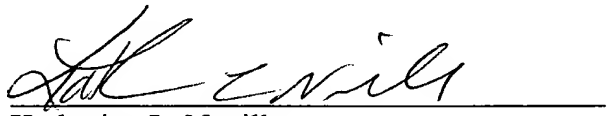
By: 

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